

Main Group Metals in Organic Synthesis

Edited by

Hisashi Yamamoto and Koichiro Oshima



WILEY-
VCH

WILEY-VCH Verlag GmbH & Co. KGaA

**Main Group Metals
in Organic Synthesis**

*Edited by
Hisashi Yamamoto and Koichiro Oshima*

Further Titles of Interest

B. Cornils and W.A. Herrmann (Eds.)

Applied Homogeneous Catalysis with Organometallic Compounds

A Comprehensive Handbook in Three Volumes

2002. ISBN 3-527-30434-7

I. Marek (Ed.)

Titanium and Zirconium in Organic Synthesis

2000. ISBN 3-527-30428-2

K. Drauz and H. Waldmann (Eds.)

Enzyme Catalysis in Organic Synthesis

A Comprehensive Handbook in Three Volumes

2002. ISBN 3-527-29949-1

K.C. Nicolaou, R. Hanco and W. Hartwig (Eds.)

Handbook of Combinatorial Chemistry

Drugs, Catalysts, Materials (Two Volumes)

2002. ISBN 3-527-30509-2

H. Yamamoto (Ed.)

Lewis Acids in Organic Synthesis

A Comprehensive Handbook in Three Volumes

2000. ISBN 3-527-29579-8

Main Group Metals in Organic Synthesis

Edited by

Hisashi Yamamoto and Koichiro Oshima



WILEY-
VCH

WILEY-VCH Verlag GmbH & Co. KGaA

Editors

Prof. Dr. Hisashi Yamamoto

University of Chicago
Department of Chemistry
5735 s Ellis Ave.
Chicago, IL 60637
USA

Prof. Dr. Koichiro Oshima

Graduate School of Engineering
Dept. of Material Chemistry
Kyoto University
Kyoto-daigaku Katsura
Nishikyo-ku
Kyoto 615-8510
Japan

■ This book was carefully produced. Nevertheless, editors, authors and publisher do not warrant the information contained therein to be free of errors. Readers are advised to keep in mind that statements, data, illustrations, procedural details or other items may inadvertently be inaccurate.

Library of Congress Card No.: Applied for.

British Library Cataloguing-in-Publication Data

A catalogue record for this book is available from the British Library.

**Bibliographic information published
by Die Deutsche Bibliothek**

Die Deutsche Bibliothek lists this publication in the Deutsche Nationalbibliografie; detailed bibliographic data is available in the Internet at <<http://dnb.ddb.de>>

© 2004 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim, Germany

All rights reserved (including those of translation in other languages). No part of this book may be reproduced in any form – by photoprinting, microfilm, or any other means – nor transmitted or translated into machine language without written permission from the publishers. Registered names, trademarks, etc. used in this book, even when not specifically marked as such, are not to be considered unprotected by law.

Printed in the Federal Republic of Germany

Printed on acid-free paper

Composition K+V Fotosatz GmbH, Beerfelden

Printing Strauss Offsetdruck GmbH, Mörlenbach

Bookbinding Litges & Dopf Buchbinderei GmbH, Heppenheim

ISBN 3-527-30508-4

Contents

Volume 1

Preface XVII

List of Contributors XIX

1	Lithium in Organic Synthesis	1
	<i>Katsuhiko Tomooka and Masato Ito</i>	
1.1	Introduction	1
1.2	Nature of Organolithium Compounds	2
1.2.1	Overview	2
1.2.2	Structural Features	4
1.2.3	Configurational Stability	5
1.2.4	Titration of Organolithium Compounds	6
1.3	Methods for the Preparation of Organolithium Compounds	8
1.3.1	Overview	8
1.3.2	Reductive Lithiation using Lithium Metal	9
1.3.3	Preparation of Organolithium Compounds from Another Organolithium Compounds	10
1.3.3.1	Deprotonation	10
1.3.3.2	Halogen–Lithium Exchange	12
1.3.3.3	Transmetallation	13
1.3.3.4	Carbolithiation	14
1.3.3.5	Miscellaneous	16
1.4	Methods for Construction of Carbon Frameworks by Use of Organolithium Compounds	21
1.4.1	Overview	21
1.4.2	Stereospecificity	21
1.4.3	Synthetic Application	23
1.4.3.1	C–C Bond Formation: Conversion of C–Li to Halogen–Li	23
1.4.3.2	C–C Bond Formation: Conversion of C–Li to O–Li	25
1.4.3.3	C–C Bond Formation: Conversion of C–Li to N–Li	29
1.5	References	32

2	Rubidium and Cesium in Organic Synthesis	35
	<i>Seiji Matsubara</i>	
2.1	Introduction	35
2.2	Organo-, Silyl-, Germyl-, and Stannylmetal	35
2.3	Fluoride Ion Source	36
2.3.1	Nucleophilic Fluorination	37
2.3.2	Desilylation Reactions	37
2.3.2.1	Carbanion Equivalent Formation	38
2.3.2.2	Desilylation-Elimination	40
2.4	Electrophilic Fluorination – Cesium Fluorosulfate	41
2.5	Cesium Salts as Bases	43
2.6	Cesium Enolate	46
2.7	Catalytic Use	47
2.8	Conclusion	49
2.9	References	49
3	Magnesium in Organic Synthesis	51
	<i>Atsushi Inoue and Koichiro Oshima</i>	
3.1	Introduction	51
3.2	Preparation of Organomagnesium Compounds	52
3.2.1	Preparation from Alkyl Halides and Mg Metal	52
3.2.2	Preparation with Rieke Magnesium	54
3.2.3	Transmetalation	55
3.2.4	Sulfoxide-Magnesium Exchange (Ligand Exchange Reaction of Sulfoxides with Grignard Reagent)	56
3.2.5	Hydromagnesation	61
3.2.6	Metalation (Deprotonation from Strong Carbon Acids)	63
3.2.7	Other Preparative Methods	64
3.3	Reaction of Organomagnesium Compounds	66
3.3.1	Reaction with Organomagnesium Amides	66
3.3.1.1	Preparation of Magnesium Monoamides and Bisamides	66
3.3.1.2	Reaction with Organomagnesium Amide	67
3.3.2	Cp ₂ TiCl ₂ - or Cp ₂ ZrCl ₂ -catalyzed Reaction with Grignard Reagents	72
3.3.3	Substitution at Carbon by Organomagnesium Compounds	76
3.3.4	Addition to Carbon-Carbon Multiple Bonds	83
3.3.5	Addition of Organomagnesium Compounds to Carbonyl Groups	88
3.4	Halogen-Magnesium Exchange Reactions	90
3.4.1	Practical Examples of Halogen-Magnesium Exchange Reactions	91
3.4.1.1	Perfluoro Organomagnesium Reagents	91
3.4.1.2	Polyhalogenated Arylmagnesium Reagents	92
3.4.1.3	Exchange of Polyhalomethane Derivatives	95
3.4.1.4	Preparation of Magnesiated Nitrogen-Heterocycles	95
3.4.1.5	Formation of Enolates by Halogen-Magnesium Exchange	98
3.4.1.6	Miscellaneous Reactions	102

- 3.4.2 *i*PrMgBr-induced Halogen-Magnesium Exchange for the Preparation of Polyfunctional Organomagnesium Reagents 104
 - 3.4.2.1 Exchange Reaction of Aryl Halides 104
 - 3.4.2.2 Exchange Reaction of Heterocyclic Halides 106
 - 3.4.2.3 Exchange Reaction of Alkenyl Halides 108
 - 3.4.2.4 Halogen-Magnesium Exchange of Other Halides 110
 - 3.4.2.5 Halogen-Magnesium Exchange of Resin-bound Halides 111
- 3.4.3 Trialkylmagnesium-induced Halogen-Magnesium Exchange Reaction 113
 - 3.4.3.1 Iodine-Magnesium Exchange of Aryl Iodides 113
 - 3.4.3.2 Bromine-Magnesium Exchange of Aryl Bromides 113
 - 3.4.3.3 Halogen-Magnesium Exchange of Dihaloarenes 117
 - 3.4.3.4 Halogen-Magnesium Exchange of Halopyridines 118
 - 3.4.3.5 Halogen-Magnesium Exchange of Alkenyl Halides 118
- 3.4.4 Bromine-Magnesium Exchange of *gem*-Dibromo Compounds and Subsequent Migration of an Alkyl Group 120
 - 3.4.4.1 Reaction of *gem*-Dibromocyclopropanes 120
 - 3.4.4.2 Copper(I)-catalyzed Reaction of Dibromomethylsilanes 122
 - 3.4.4.3 Reaction of Dibromomethylsilanes with Me₃MgLi 123
 - 3.4.4.4 Alkylation of Carbenoids with Grignard Reagents 123
- 3.5 Radical Reactions Mediated by Grignard Reagents 124
 - 3.5.1 Cross-coupling of Alkyl Halides with Grignard Reagents 125
 - 3.5.2 Conversion of Vicinal Methoxyiodoalkanes into (*E*)-Alkenes with Grignard Reagent 127
 - 3.5.3 Radical Cyclization of β -Iodo Allylic Acetals with EtMgBr 127
 - 3.5.4 EtMgBr-iodoalkane-mediated Coupling of Arylmagnesium Compounds with Tetrahydrofuran via a Radical Process 128
 - 3.5.5 Mg-promoted Reductive Cross-coupling of α,β -Unsaturated Carbonyl Compounds with Aldehydes or Acyl Chlorides 131
- 3.6 Radical Reaction Mediated by Grignard Reagents in the Presence of Transition Metal Catalyst 134
 - 3.6.1 Titanocene-catalyzed Double Alkylation or Double Silylation of Styrenes with Alkyl Halides or Chlorosilanes 134
 - 3.6.2 Reaction of Grignard Reagents with Organic Halides in the Presence of Cobaltous Chloride 138
 - 3.6.3 Cobalt-catalyzed Aryl Radical Cyclizations with Grignard Reagent 139
 - 3.6.4 Cobalt-catalyzed Phenylative Radical Cyclization with Phenyl Grignard Reagent 140
 - 3.6.5 Cobalt-catalyzed Heck-type Reaction of Alkyl Halides with Styrenes 142
 - 3.6.6 Radical Cyclization of β -Halo Allylic Acetal with a Grignard Reagent in the Presence of Manganese(II) Chloride or Iron(II) Chloride 146
- 3.7 References 150

4	Calcium in Organic Synthesis 155
	<i>Jih Ru Hwu and Ke-Yung King</i>
4.1	Introduction 155
4.2	Reductive Cleavage of Various C–O Bonds 155
4.2.1	O-Debenzylation 155
4.2.2	Cleavage of the (O=C)–OAc Single Bond 157
4.2.3	Cleavage of the R ₂ N(O=C)C–O(C=O)R Single Bond 159
4.2.4	Cleavage of the C–O Bond in Dihydropyrans 160
4.2.5	Conversion of Epoxides to Alcohols 160
4.3	Reductive Cleavages of Various C–S Bonds 161
4.3.1	Desulfonylation 161
4.3.2	Cleavage of an (R ₂ NCO)C–S Bond 162
4.3.3	Removal of Dithiolanes from an Allylic Position 162
4.4	Reductive Cleavage of Various C–N Bonds 163
4.4.1	Cleavage of a PhC–N Bond 163
4.4.2	Reduction of Nitriles 165
4.5	Reduction of C=C and C≡C Bonds 165
4.5.1	Reduction of Alkynes 165
4.5.2	Reduction of Strained C=C Bonds 166
4.5.3	Reduction of Aryl Rings 166
4.6	Calcium Reagents in Different Forms in the Reduction of Organic Halides 167
4.7	Reductive Cleavage of an N–O Bond 168
4.8	Reduction of Various Types of Functional Group 169
4.9	Chemoselectivity and Limitation 169
4.10	Conclusions 173
4.11	Acknowledgment 173
4.12	References 173
5	Barium in Organic Synthesis 175
	<i>Akira Yanagisawa</i>
5.1	Introduction 175
5.2	Reactive Barium-promoted Carbon–Carbon Bond-forming Reactions 175
5.3	Preparation of Allylic Barium Reagents and Reactions of these Carbanions with Electrophiles 177
5.4	Other Carbon–Carbon Bond-forming Reactions Promoted by Barium Compounds 185
5.5	Summary and Conclusions 187
5.6	References 188
6	Aluminum in Organic Synthesis 189
	<i>Susumu Saito</i>
6.1	Introduction 189
6.1.1	Natural Abundance and General Properties 190
6.1.2	Interaction of Aluminum(III) with Different Functional Groups 190

6.1.2.1	Coordination and Covalent Bonds in Aluminum(III)	190
6.1.2.2	Cationic Aluminum(III): Structural and Reaction Features	192
6.1.2.3	Neutral Aluminum(III): Coordination Aptitude and Molecular Recognition	196
6.1.2.4	Other Novel Interactions Involving Neutral Aluminum(III)	203
6.1.2.5	Ligand Effect on Aluminum(III) Geometry and Interactions	206
6.2	Modern Aluminum Reagents in Selective Organic Synthesis	208
6.2.1	Carbon–Carbon Bond Formation	208
6.2.1.1	Generation and Reaction of Aluminum Enolates (Al–O–C=C Bond Formation and Reaction)	208
6.2.1.2	Aluminum–Carbonyl Complexation, Activation, and Nucleophilic Reaction	220
6.2.1.3	Strecker Reaction (Addition of CN [−] to C=N Bonds)	257
6.2.1.4	Carboalumination (Addition of Al–C Bonds to C=C and CC≡Bonds)	258
6.2.1.5	Coupling Reactions using Transition Metals (Addition of Al–C Bonds to Other Metals and Reductive Elimination)	263
6.2.2	Reduction	264
6.2.2.1	Carbonyl Reduction (H [−] Addition to a C=O Bond)	265
6.2.2.2	Hydroalumination (H [−] Addition to C=C or CC≡Bonds)	267
6.2.3	Oxidation	271
6.2.4	Rearrangement and Fragmentation	273
6.2.4.1	Beckmann Rearrangement	273
6.2.4.2	Epoxide Rearrangement	274
6.2.4.3	Claisen Rearrangement	275
6.2.4.5	Other Rearrangements and Fragmentation	278
6.2.5	Radical Initiation and Reactions	279
6.2.6	Polymerization	283
6.2.6.1	Anionic Polymerization	284
6.2.6.2	Radical Polymerization	291
6.2.6.3	Cationic Polymerization	291
6.3	Conclusion	299
6.4	References	300
7	Gallium in Organic Synthesis	307
	<i>Masahiko Yamaguchi</i>	
7.1	Use as Lewis Acids	307
7.2	Use as Bases	311
7.3	Use as Organometallic Alkylating Reagents	312
7.3.1	Carbonyl Addition Reaction	312
7.3.2	Cross-coupling Reactions	315
7.3.3	Carbometalation Reactions	316
7.4	Use as Radical Reagents	319
7.5	Use as Low Valence Reagents	320
7.6	References	321

8	Indium in Organic Synthesis 323
	<i>Shuki Araki and Tsunehisa Hirashita</i>
8.1	Introduction 323
8.2	Allylation and Propargylation 324
8.2.1	Allylation and Propargylation of Carbonyl Compounds 325
8.2.1.1	Regioselectivity 325
8.2.1.2	Diastereoselectivity 327
8.2.1.3	Enantioselectivity 334
8.2.1.4	Other Allylation Reactions 335
8.2.2	Allylation and Propargylation of Compounds other than Carbonyl 338
8.2.2.1	Imines and Enamines 338
8.2.2.2	Alkenes and Alkynes 340
8.2.2.3	Other Compounds 343
8.3	Reformatsky and Other Reactions 346
8.4	Reactions in Combination with Transition-metal Catalysts 348
8.5	Reduction 354
8.5.1	Reduction of Carbonyl Groups 354
8.5.2	Reductive Coupling 356
8.5.3	Dehalogenation 358
8.5.4	Reduction of Functional Groups 360
8.6	Indium Salts as Lewis Acids 364
8.6.1	The Diels-Alder Reaction 364
8.6.2	Aldol and Mannich Reactions 366
8.6.3	Michael Addition 368
8.6.4	Friedel-Crafts Reaction 369
8.6.5	Heterocycle Synthesis 371
8.6.6	Miscellaneous Reactions 376
8.7	References 379
9	Thallium in Organic Synthesis 387
	<i>Sakae Uemura</i>
9.1	Tl(III) Salts in Organic Synthesis 388
9.1.1	Alkene Oxidations 388
9.1.2	Ketone Oxidations 392
9.1.3	Aromatic Thallation 395
9.1.4	Aryl Couplings via One-electron Transfer 397
9.1.5	Phenol Oxidations 398
9.1.6	Miscellaneous Reactions and Catalytic Reactions 400
9.2	Tl(I) Salts in Organic Synthesis 403
9.3	References 406

Volume 2

10	Silicon in Organic Synthesis 409 <i>Katsukiyo Miura and Akira Hosomi</i>
10.1	Introduction 409
10.2	Silyl Enolates 409
10.2.1	Aldol Reactions 410
10.2.1.1	Achiral Lewis Acid-promoted Reactions in Anhydrous Solvent 410
10.2.1.2	Aqueous Aldol Reaction with Water-stable Lewis Acids 423
10.2.1.3	Aldol Reactions via Activation of Silyl Enolates 425
10.2.1.4	New Types of Silyl Enolate 426
10.2.2	Asymmetric Aldol Reactions 434
10.2.2.1	Use of a Chiral Auxiliary 434
10.2.2.2	Use of Chiral Lewis Acids and Transition Metal Complexes 434
10.2.2.3	Use of Chiral Fluoride Ion Sources 453
10.2.2.4	Use of Trichlorosilyl Enolates and Chiral Lewis Bases 455
10.2.3	Carbonyl–Ene Reactions 456
10.2.4	Mannich-type Reactions 457
10.2.4.1	Achiral Brønsted and Lewis Acid-promoted Reactions 458
10.2.4.2	Base-catalyzed Reactions 462
10.2.4.3	Asymmetric Mannich-type Reactions 463
10.2.5	Mukaiyama–Michael Reactions 467
10.2.5.1	Achiral Lewis Acid-promoted Reactions 468
10.2.5.2	Solvent-promoted Reactions 471
10.2.5.3	Asymmetric Michael Reactions 471
10.2.6	Alkylation and Allylation of Silyl Enolates 473
10.2.7	Vinylation and Arylation of Silyl Enolates 476
10.2.8	Acylation of Silyl Enolates 480
10.2.9	Diels–Alder Reactions of Siloxy-substituted 1,3-Diene 480
10.2.9.1	New Types of Siloxy-substituted 1,3-Diene 482
10.2.9.2	Achiral Brønsted and Lewis Acid-promoted Reactions 484
10.2.9.3	Asymmetric Reactions using Chiral Auxiliaries 486
10.2.9.4	Catalytic Asymmetric Reactions with Alkenes 487
10.2.9.5	Catalytic Asymmetric Reactions with Heterodienophiles 487
10.3	Allylsilanes, Allenylsilanes, and Propargylsilanes 489
10.3.1	Allylation, Propargylation, and Allenylation of Carbon Electrophiles 490
10.3.1.1	Lewis Acid-promoted Reactions of Aldehydes, Ketones, and Acetals 491
10.3.1.2	New Types of Allylation Reaction of Carbonyl Compounds 496
10.3.1.3	Asymmetric Reactions of Aldehydes, Ketones, and Acetals 499
10.3.1.4	Allylation of Carbon–Nitrogen Double Bonds 505
10.3.1.5	Conjugate Addition to α,β -unsaturated Carbonyl Compounds 509
10.3.1.6	Tandem Reactions Including Two or More Carbon–Carbon Bond-forming Processes 511

10.3.2	Ene Reactions of Allylsilanes	514
10.3.3	Lewis Acid-promoted Cycloadditions	515
10.3.3.1	Cycloadditions with 1,2-Silyl Migration	516
10.3.3.2	[2+2] Cycloadditions	523
10.3.3.3	Other Cycloadditions without 1,2-Silyl Migration	525
10.3.4	Lewis Acid-catalyzed Carbosilylation of Unactivated Alkynes and Alkenes	529
10.3.5	Metal-promoted Allylation of Alkynes and Dienes	531
10.3.6	Homolytic Allylation	532
10.4	Vinylsilanes, Arylsilanes, and Alkynylsilanes	534
10.4.1	Lewis Acid-promoted Electrophilic Substitution	534
10.4.2	Lewis Acid-promoted Reactions Forming Silylated Products	535
10.4.3	Transition Metal-catalyzed Carbon–Carbon Bond Formation	537
10.4.3.1	Palladium-catalyzed Reactions	537
10.4.3.2	Rhodium-catalyzed Reactions	540
10.4.3.3	Copper-promoted Reactions	541
10.5	α -Heteroatom-substituted Organosilanes	542
10.5.1	Nucleophile-promoted Addition of α -Halo- and α -Thioalkylsilane	543
10.5.2	[3+2] Cycloadditions of Silyl-protected 1,3-Dipoles	544
10.5.3	Carbon–Carbon Bond Formation with Acylsilanes	545
10.5.3.1	Tandem Carbon–Carbon Bond Formation via Brook Rearrangement	546
10.5.3.2	Transition Metal-catalyzed Acylation	547
10.5.3.3	Radical Addition Followed by Brook-type Rearrangement	549
10.5.4	Carbon–Carbon Bond Formation with Cyanosilanes	550
10.5.4.1	Cyanosilylation using Achiral Catalysts	551
10.5.4.2	Asymmetric Cyanosilylation of Aldehydes and Ketones	553
10.5.4.3	Asymmetric Hydrocyanation of Imines	556
10.5.4.4	Asymmetric Desymmetrization of <i>meso</i> Epoxides	557
10.5.4.5	Transition Metal-catalyzed Reactions	558
10.6	Silicon-containing Strained Molecules	561
10.6.1	Carbon–Carbon Bond Formation with Silacyclopropanes	561
10.6.2	Carbon–Carbon Bond Formation with Silacyclobutanes	564
10.7	References	568
11	Germanium in Organic Synthesis	593
	<i>Takahiko Akiyama</i>	
11.1	Introduction	593
11.2	Allylgermanes	593
11.2.1	Preparation	593
11.2.2	Reaction	594
11.3	Germanium–Hydrogen Bonds (Reductive Radical Chain Reactions)	598
11.4	Transition Metal-catalyzed Addition of Ge–X to an Unsaturated Bond	603
11.4.1	Hydrogermylation	603

- 11.4.2 Carbogermylation 604
- 11.4.3 Germymetalation 605
- 11.5 Germanium–Metal Bonds 605
- 11.6 Vinylgermane [69] 609
- 11.7 Alkynylgermanes and Arylgermanes [74] 611
- 11.8 Acylgermanes [81] 613
 - 11.8.1 Preparation 613
 - 11.8.2 Reactions 614
- 11.9 Germanium Enolate 615
- 11.10 Miscellaneous 615
- 11.11 References 616

- 12 Tin in Organic Synthesis 621**
Akihiro Orita and Junzo Otera
 - 12.1 Introduction 621
 - 12.2 Allylstannanes 622
 - 12.2.1 Mechanistic Aspects of Allylation of Aldehydes with Allylic Stannanes 622
 - 12.2.2 Allylic Stannanes as Allylating Reagents 625
 - 12.2.3 For Easy Separation from Tin Residues 629
 - 12.2.4 Activation of Allylstannanes by Transmetalation 630
 - 12.2.5 Asymmetric Allylation 635
 - 12.2.6 Free Radical Reactions using Allylstannanes 639
 - 12.3 Sn–Li Exchange 641
 - 12.4 Migita-Kosugi-Stille Coupling 653
 - 12.5 Organotin Hydrides 671
 - 12.5.1 Selective Reduction of Functional Groups 673
 - 12.5.2 Free-radical C–C Bond Formation 682
 - 12.6 Organotin Enolate 688
 - 12.7 Organotin Alkoxides and Halides 691
 - 12.7.1 Utilization of Sn–O Bonds in Synthetic Organic Chemistry 691
 - 12.7.2 Transesterification 698
 - 12.7.3 Organotin in Lewis Acids 705
 - 12.8 References 708

- 13 Lead in Organic Synthesis 721**
Taichi Kano and Susumu Saito
 - 13.1 Introduction 721
 - 13.1.1 General Aspects 721
 - 13.1.2 Preparation of Organolead Compounds 722
 - 13.1.3 Outstanding Features of Lead Compounds 722
 - 13.2 Pb(IV) Compounds as Oxidizing Agents [Pb(IV) is Reduced to Pb(II)] 724
 - 13.2.1 C–C Bond Formation (Alkylation, Arylation, Vinylation, Acetylenation, C–C Coupling, etc.) 724

13.2.1.1	Arylation of Enolate Equivalents	724
13.2.1.2	Vinylation of Enolate Equivalents	728
13.2.1.3	Alkynylation of Enolate Equivalents	729
13.2.1.4	Aryl–Aryl Coupling	729
13.2.1.5	Other C–C Bond-forming Reactions (R–Pb as R [•] or R [−])	732
13.2.1.6	Transition Metal-catalyzed Reactions	733
13.2.1.7	C–C Bond-forming Reactions using Pb(OAc) ₄	734
13.2.2	C–O Bond Formation (Acetoxylation, Including Oxidative Cleavage of a C–Si Bond, etc.)	735
13.2.3	C–N Bond Formation (Aziridination, etc.)	738
13.2.4	C–X (Cl, Br, I) Bond Formation	741
13.2.5	C–C Bond Cleavage (Fragmentation: Cyclic to Acyclic, etc.)	741
13.3	Pb(II) as a Lewis Acid	744
13.4	Pb(0) Compounds as Reducing Agents [Pb(0) is Oxidized to Pb(II); Catalytic Use of Pb(II), etc.]	746
13.5	Conclusion	748
13.6	References	748
14	Antimony and Bismuth in Organic Synthesis	753
	<i>Yoshihiro Matano</i>	
14.1	Introduction	753
14.2	Antimony in Organic Synthesis	755
14.2.1	Elemental Antimony and Antimony(III) Salts	755
14.2.1.1	Carbon–Carbon Bond-forming Reactions	755
14.2.1.2	Carbon–Heteroatom Bond-forming Reactions	756
14.2.1.3	Reduction	757
14.2.1.4	Miscellaneous Reactions	758
14.2.2	Antimony(V) Salts	758
14.2.2.1	Carbon–Carbon Bond-forming Reactions	758
14.2.2.2	Carbon–Heteroatom Bond-forming Reactions	762
14.2.2.3	Oxidation	764
14.2.2.4	Reduction	765
14.2.2.5	Miscellaneous Reactions	766
14.2.3	Organoantimony(III) Compounds	766
14.2.3.1	Carbon–Carbon Bond-forming Reactions	766
14.2.3.2	Carbon–Heteroatom Bond-forming Reactions	769
14.2.3.3	Oxidation	769
14.2.3.4	Reduction	770
14.2.3.5	Miscellaneous Reactions	770
14.2.4	Organoantimony(V) Compounds	770
14.2.4.1	Carbon–Carbon Bond-forming Reactions	770
14.2.4.2	Carbon–Heteroatom Bond-forming Reactions	772
14.2.4.3	Oxidation	774
14.2.4.4	Miscellaneous Reactions	774

14.3	Bismuth in Organic Synthesis	775
14.3.1	Elemental Bismuth and Bismuth(III) Salts	775
14.3.1.1	Carbon–Carbon Bond-forming Reactions	775
14.3.1.2	Carbon–Heteroatom Bond-forming Reactions	779
14.3.1.3	Oxidation	783
14.3.1.4	Reduction	784
14.3.1.5	Miscellaneous Reactions	786
14.3.2	Bismuth(V) Salts	787
14.3.2.1	Oxidation	787
14.3.2.2	Miscellaneous Reactions	788
14.3.3	Organobismuth(III) Compounds	788
14.3.3.1	Carbon–Carbon Bond-forming Reactions	788
14.3.3.2	Carbon–Heteroatom Bond-forming Reactions	790
14.3.3.3	Oxidation	792
14.3.4	Organobismuth(V) Compounds	792
14.3.4.1	Carbon–Carbon Bond-forming Reactions	792
14.3.4.2	Carbon–Heteroatom Bond-forming Reactions	796
14.3.4.3	Oxidation	798
14.3.4.4	Miscellaneous Reactions	799
14.4	References	799
15	Selenium and Tellurium in Organic Synthesis	813
	<i>Akiya Ogawa</i>	
15.1	Introduction	813
15.2	Preparation of Parent Selenium and Tellurium Compounds	813
15.2.1	General Aspects of Selenium and Tellurium Compounds	813
15.2.2	Parent Selenium Compounds	815
15.2.2.1	Hydrogen Selenide and its Metal and Amine Salts	815
15.2.2.2	Selenols and their Metal Salts	816
15.2.2.3	Selenides and Diselenides	817
15.2.2.4	Selenenic Acids and their Derivatives	819
15.2.2.5	Seleninic Acids and their Derivatives	821
15.2.3	Parent Tellurium Compounds	821
15.2.3.1	Hydrogen Telluride and its Metal Salts	821
15.2.3.2	Tellurols and their Metal Salts	822
15.2.3.3	Tellurides and Ditellurides	823
15.2.3.4	Tellurenyl Compounds	824
15.2.3.5	Tellurinyl Compounds	825
15.3	Selenium Reagents as Electrophiles	826
15.3.1	Electrophilic Addition to Unsaturated Bonds	826
15.3.2	Cyclofunctionalization	828
15.3.3	Synthesis of α,β -Unsaturated Carbonyl Compounds via α -Seleno Carbonyl Compounds	830
15.3.4	Polymer-supported or Fluorous Selenium Reagents	830
15.3.5	Selenium-catalyzed Carbonylation with CO	831

15.4	Radical Reactions of Selenium and Tellurium Compounds	832
15.4.1	Organoselenium Compounds as Carbon Radical Precursors	832
15.4.1.1	Group-transfer Reactions of Organoselenium Compounds	833
15.4.1.2	Group-transfer Reaction of Organotellurium Compounds	835
15.4.2	Addition of Selenium- and Tellurium-centered Radicals	835
15.4.2.1	Radical Addition of Selenols and Diselenides to Alkynes and Allenes	838
15.4.2.2	Radical Addition to Alkenes	841
15.5	Selenium and Tellurium Reagents as Nucleophiles	843
15.5.1	Selenium-stabilized Carbanions	843
15.5.2	Tellurium-lithium Exchange Reaction	844
15.6	Transition Metal-catalyzed Reactions	845
15.6.1	Cross-coupling Reaction	846
15.6.2	Transition Metal-catalyzed Addition Reaction	847
15.6.3	Transition Metal-catalyzed Carbonylation Reaction	850
15.7	Reduction and Oxidation Reactions	851
15.7.1	Reduction Reactions	851
15.7.1.1	Reduction of Selenium and Tellurium Compounds	851
15.7.1.2	Reduction using Hydrogen Selenide and Selenols and their Tellurium Analogs	851
15.7.1.3	Reduction with Selenolates and Tellurolates	852
15.7.2	Oxidation Reactions	852
15.7.2.1	Selenium Dioxide Oxidation	852
15.7.2.2	Selenoxide <i>syn</i> Elimination	854
15.7.2.3	[2,3]Sigmatropic Rearrangement	855
15.7.2.4	Seleninic Acid Oxidation	855
15.8	References	855

Subject Index 867

Preface

Historically, main-group organometallics and metallorganics have played a major role in modern organic synthesis. The Grignard reagent has played quite a significant role in this field of chemistry for more than one hundred years. For most chemists, this type of magnesium compound is probably the first organometallic reagent that is encountered in their first organic-chemistry course. Although the use of Grignard reagents is truly impressive, the actual mechanistic details of reactions of these well-known organometallic compounds are still vague. Recent advances in various analytical technologies have allowed us to understand some of details of reactions that use the classical reagent. In light of the elucidation of various mechanisms, we now recognize the role of Grignard reagents in organic synthesis to be even greater than first anticipated.

Now that we are able to understand the chemical behavior of many main-group elements such as lithium, silicon, boron, and aluminum, the purpose of this book is to summarize these recent developments and show the promising future roles of complexes of these metals in modern organic synthesis. In fact, these reagents are both useful and much safer than most transition-metal compounds.

This volume focuses on areas of main-group organometallic and metallorganic reagents selected for their significant development during the last decade. Each author is very knowledgeable in their particular field of chemistry, and is able to provide a valuable perspective from a synthetic point of view. We are grateful to the distinguished chemists for their willingness to devote their time and effort to provide us with these valuable contributions.

Hisashi Yamamoto and Koichiro Oshima
Chicago and Kyoto

List of Contributors

Takahiko Akiyama
Department of Chemistry,
Faculty of Science
Gakushuin University
1-5-1 Mejiro
Toshima-ku
Tokyo 171-8588
Japan

SHUKI ARAKI
Department of Applied Chemistry
Nagoya Institute of Technology
Gokiso-cho
Showa-ku
Nagoya 466-8555
Japan

AKIRA HOSOMI
Department of Chemistry
University of Tsukuba
Tsukuba, Ibaraki 305-8571
Japan

J. R. HWU
Department of Chemistry
National Tsing Hua University
Hsinchu
Taiwan 30043

ATSUSHI INOUE
Department of Material Chemistry
Graduate School of Engineering
Kyoto University
Yoshida Hommachi
Sakyo-Ku
Kyoto 606-8501
Japan

MASATO ITO
Department of Applied Chemistry
Tokyo Institute of Technology
Meguro-ku
Tokyo 152-8552
Japan

TAICHI KANO
Graduate School of Engineering
Nagoya University
Chikusa
Nagoya 464-8603
Japan
E-mail: susumu@cc.nagoya-u.ac.jp

YOSHIHIRO MATANO
Department of Molecular Engineering
Graduate School of Engineering
Kyoto University
Kyoto-daigaku Katsura
Nishikyo-ku
Kyoto 615-8510
Japan

SEJIRO MATSUBARA
Department of Material Chemistry
Graduate School of Engineering
Kyoto University
Kyoto-daigaku Katsura
Nishikyo-ku
Kyoto 615-8510
Japan

KATSUKIYO MIURA
Department of Chemistry
University of Tsukuba
Tsukuba
Ibaraki 305-8571
Japan

AKIYA OGAWA
Department of Chemistry
Faculty of Science
Nara Woman's University
Kitauoyanishi-machi
Nara 630-8506
Japan

AKIHIRO ORITA
Department of Applied Chemistry
Okayama University of Science
Ridai-cho
Okayama 700-0005
Japan

KOISHIRO OSHIMA
Department of Material Chemistry
Graduate School of Engineering
Kyoto University
Kyoto-daigaku Katsura
Nishikyo-ku
Kyoto 615-8510
Japan

JUNZO OTERA
Department of Applied Chemistry
Okayama University of Science
Ridai-cho
Okayama 700-0005
Japan

SUSUMU SAITO
Graduate School of Engineering
Nagoya University
Chikusa
Nagoya 464-8603
Japan

KATSUHIKO TOMOOKA
Department of Applied Chemistry
Tokyo Institute of Technology
Meguro-ku
Tokyo 152-8552
Japan

SAKAE UEMURA
Department of Energy
and Hydrocarbon Chemistry
Graduate School of Engineering
Kyoto University
Kyoto-daigaku Katsura
Nishikyo-ku
Kyoto 615-8510
Japan

MASAHIKO YAMAGUCHI
Department of Organic Chemistry
Graduate School
of Pharmaceutical Sciences
Tohoku University
Aoba
Sendai, 980-8578
Japan

AKIRA YANAGISAWA
Department of Chemistry
Faculty of Science
Chiba University
Inage
Chiba 263-8522
Japan

1

Lithium in Organic Synthesis

KATSUHIKO TOMOOKA and MASATO ITO

1.1

Introduction

Organolithium compounds are central to many aspects of synthetic organic chemistry and are primarily used as carbanions to construct carbon skeletons of a wide variety of organic compounds. Despite the strictly anhydrous conditions generally required for successful performance of reactions using organolithium compounds, their fundamental significance in synthetic organic chemistry remains unchanged. Tremendous efforts have therefore been devoted to the development of convenient methods for generation of tailor-made organolithium compounds and useful reactions using conventional organolithium compounds.

Because comprehensive literature [1–8] covering various aspects of organolithium chemistry has recently become available, the purpose of this chapter is to highlight “powerful synthetic tools” involving organolithium compounds. The definition of “organolithium” is here limited to those compounds in which there is a clear C–Li bond; compounds with enolate or ynoate structures or with heteroatom (Y)–Li bonds, etc., have been excluded.

This chapter is roughly divided into three sections. The nature of organolithium compounds, their structures, the configurational stability of their C–Li bond, and general guidelines regarding the handling organolithium compounds are briefly considered first (Section 1.2). The next section concerns the classification of useful methods for generation of organolithium compounds in which new C–Li bonds are created either by reduction, using lithium metal itself, or by the conversion of a C–Li bond into a less reactive C–Li bond (Section 1.3). The last section primarily describes potential methods for construction of the carbon framework, driven by conversion of a C–Li bond into a less reactive Y–Li bond (Section 1.4). All the examples dealt with in the last two sections have been selected on the basis of the distinct advantages of employing organolithium compounds compared with other organometallic reagents. We will not detail pioneering works underlying the establishment of selected examples, because we are concerned that excessive comprehensiveness might obscure their marked synthetic importance. There is no doubt, however, that modern synthetic technology has been developed on the basis of the considerable efforts of our forefathers, and readers are strongly recommended to

refer to other books or reviews cited in this chapter for historical aspects and other issues regarding organolithium chemistry.

1.2

Nature of Organolithium Compounds

1.2.1

Overview

Because organolithium compounds are generally sensitive to oxygen and moisture, rigorous exclusion is required to prevent decomposition. They are, however, stable in anhydrous hydrocarbons under a nitrogen or, preferably, argon atmosphere at ambient temperature, and the solutions can be stored for longer at low-

Tab. 1.1 Commercially available organolithium compounds

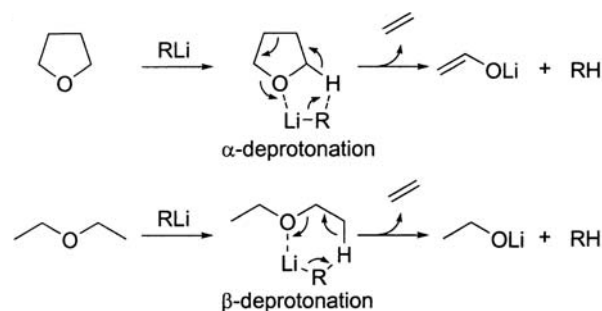
<i>Organolithium compound</i>	<i>Abbreviation</i>	<i>Solvent</i>	<i>Concn (M)</i>
Methylithium	MeLi	Diethyl ether	1.0 ^{a)}
			1.4 ^{c)}
Methylithium-lithium bromide complex	MeLi–LiBr	Diethyl ether	1.5 ^{c)}
			2.2 ^{b)}
Methylithium-lithium iodide complex	MeLi–LiI	Diethyl ether	1.0 ^{c)}
<i>n</i> -Butyllithium	<i>n</i> -BuLi	Hexane	1.6 ^{a-c)}
			2.5 ^{b, c)}
			2.6 ^{a)}
			3.0 ^{a)}
			10.0 ^{c)}
			10.0 ^{c)}
<i>s</i> -Butyllithium	<i>s</i> -BuLi	Cyclohexane	2.0 ^{c)}
		Pentane	2.0 ^{c)}
		Cyclohexane	1.0 ^{a)}
<i>t</i> -Butyllithium	<i>t</i> -BuLi	Pentane	1.3 ^{c)}
			1.4 ^{b)}
			1.5 ^{a)}
Phenyllithium	PhLi	Cyclohexane-diethyl ether	1.7 ^{c)}
			1.0 ^{a)}
Lithium acetylide-ethylene-diamine complex	HC≡CLi–H ₂ NC ₂ H ₄ NH ₂	None (powder ca. 90% purity)	1.8 ^{c)}
			1.9 ^{b)}
		Dibutyl ether	2.0 ^{b)}
			– ^{a-c)}
		Toluene	– ^{b, c)}
		(suspension 25%, w/w)	

a) Kanto Kagaku. b) Wako Chemicals. c) Sigma-Aldrich.

er temperatures [1, 2]. Simple organolithium starting materials listed in Tab. 1.1 are commercially available as solutions in such solvents. Exceptionally, the lithium acetylide-ethylenediamine complex is available as a solid. Hydrocarbon solutions of *n*-, *s*-, and *t*-BuLi are the ultimate source of most organolithium compounds, and their availability has greatly contributed to the advancement of organolithium chemistry. In general, ethereal solvents such as diethyl ether or tetrahydrofuran are most frequently used either in the preparation of organolithium compounds or in their reactions, because they reduce the extent of aggregation of organolithium compounds and hence increase their reactivity (Section 1.2.2). To increase their reactivity further, *N,N,N',N'*-tetramethylethylenediamine (TMEDA), 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidine (DMPU), or hexamethylphosphoramide (HMPA) are effective co-solvents, because of their high coordinating ability. It should be noted that organolithium compounds are thermally unstable in ethereal solvents; their half-lives [1, 9, 10] are summarized in Tab. 1.2. Thermal decomposition arises as a result of deprotonation of ethereal solvents by organo-

Tab. 1.2 Half-lives of organolithium compounds in common ethereal solvents

<i>RLi</i>	<i>Solvent</i>	-70°C	-40°C	-20°C	0°C	+20°C	+35°C
<i>t</i> -BuLi	DME	11 min					
	THF		5.6 h	42 min			
	ether			8 h	1.0 h		
<i>s</i> -BuLi	DME	2.0 h	2 min				
	THF			1.3 h			
	ether			20 h	2.3 h		
<i>n</i> -BuLi	DME			1.8 h	<5 min		
	THF				17 h	1.8 h	10 min
	ether					153 h	31 h
PhLi	ether						12 days
MeLi	ether					3 months	



Scheme 1.1

lithium compounds, because of their high basicity, leading to a variety of decomposition products with Li–O bonds, as illustrated in Scheme 1.1.

1.2.2

Structural Features

The electron-deficient lithium atom of an organolithium compound requires greater stabilization than can be provided by a single carbanionic ligand, and freezing measurements indicate that in hydrocarbon solution organolithium compounds are invariably aggregated as hexamers, tetramers, or dimers [11] (Tab. 1.3). The structures of these aggregates in solution can be deduced to some extent from the crystal structures of organolithium compounds [12] or by calculation [13]: the tetramers approximate to lithium atom tetrahedra unsymmetrically bridged by the organic ligands [4, 5]. The aggregation state of simple, unfunctionalized organolithium compounds depends primarily on steric hindrance. Primary organolithium compounds are hexamers in hydrocarbons, except when branching β to the lithium atom leads to tetramers. Secondary and tertiary organolithium compounds are tetramers whereas benzyllithium and very bulky alkyl-lithium compounds are dimers [1, 11].

Coordinating ligands such as ethers or amines, or even metal alkoxides can provide an alternative source of electron density for the electron-deficient lithium atoms. These ligands can stabilize the aggregates by coordinating to the lithium atoms at their vertices; this enables the organolithium compounds to shift to an entropically favored lower degree of aggregation. As shown in Tab. 1.3, the presence of ethereal solvents typically causes a shift down in the aggregation state, but only occasionally results in complete deaggregation to the monomer [1]. Methyl-lithium and butyllithium remain tetramers in diethyl ether, THF, or DME, with some dimers forming at low temperatures; *t*-BuLi becomes dimeric in diethyl

Tab. 1.3 Aggregation states of typical organolithium compounds

<i>RLi</i>	<i>In hydrocarbon solvent</i>	<i>In ethereal solvent</i>
MeLi	–	Tetramer
EtLi	Hexamer	Tetramer
<i>n</i> -BuLi	Hexamer	Tetramer
<i>i</i> -BuLi	Tetramer	–
BnLi	Dimer	Monomer
<i>i</i> -PrLi	Tetramer	Dimer
<i>s</i> -BuLi	–	Dimer
PhLi	–	Dimer
<i>t</i> -BuLi	Tetramer	Dimer

ether and monomeric in THF at low temperatures [14–17]. Coordinating solvents also greatly increase the reactivity of the organolithium compounds, and an ether or amine solvent is indispensable in almost all organolithium reactions.

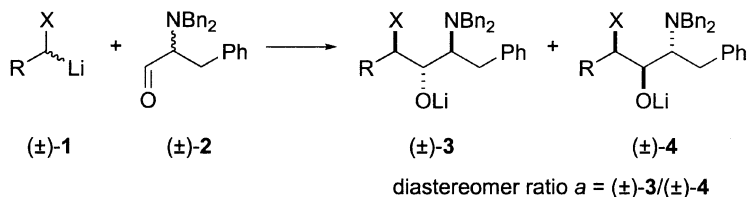
1.2.3

Configurational Stability

In principle, the configurational stability at the metal-bearing stereogenic carbon in organometallic compounds decreases as the ionic character of the carbon–metal bond increases. Because organolithium compounds contain one of the most electropositive elements some charge separation occurs in their C–Li bonds. Coordinating solvents greatly enhance the extent of charge separation. Enantio-enriched organolithium compounds, if successfully generated, usually, therefore, undergo racemization, which can be explained by migration of the Li cation from one face of the anion to the other. For example, the half-lives for racemization of secondary, unfunctionalized organolithium compounds in diethyl ether are only seconds at -70°C , even though those in non-polar solvents can be lengthened to hours at -40°C and to minutes at 0°C [18]. Accordingly, the design of stereoselective reactions with enantio-enriched organolithium compounds has long been unattractive to the synthetic organic community. The last decade, however, has witnessed a significant advance in this area, and a number of functionalized organolithium compounds with a configurationally stable C–Li bond have been found by taking advantage of the Hoffmann test [19], which provides a qualitative guide to the configurational stability of an organolithium compound.

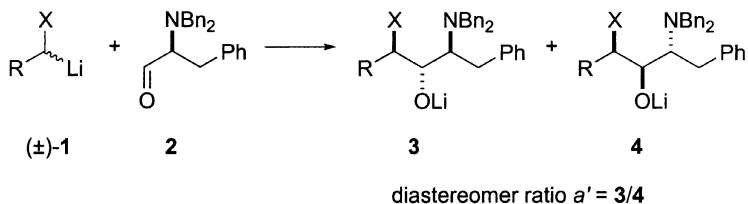
The Hoffmann test, the essence of which is described briefly below, comprises of two experiments using a suitable chiral electrophile such as an aldehyde in either the racemic or enantiomerically pure form. The occurrence of sufficient kinetic resolution on reaction of a racemic organolithium compound (\pm)-**1** with a chiral electrophile **2** is established in the first experiment by using **2** in the racemic form. In a second experiment the organolithium compound (\pm)-**1** is added to the enantiomerically pure **2** and the ratios (a and a') of the diastereomeric products **3** and **4** resulting from the two experiments are compared. If they are identical ($a = a'$) at conversions of $>50\%$, the organolithium compound **1** is configurationally labile on the time-scale set by the rate of its addition to **2**. If there is an analytically significant difference between the diastereomer ratios ($a \neq a'$), enantiomer equilibration of the organolithium compound is slower than its addition to the electrophile (Chart 1.1).

experiment I



If $a = 1$, test is insensitive.
If $a \neq 1$, go to Experiment II.

experiment II



If $a' = a$, **1** is configurationally *unstable*.
If $a' \neq a$, **1** is configurationally *stable*.

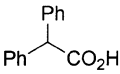
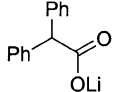
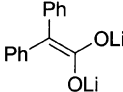
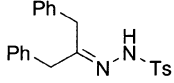
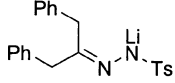
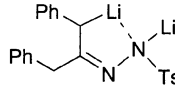
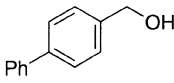
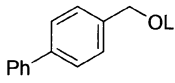
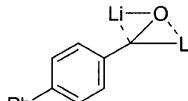
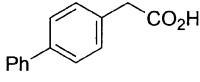
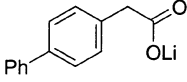
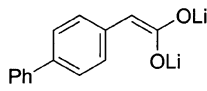
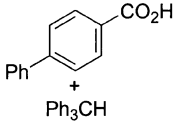
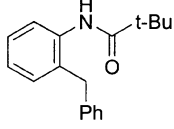
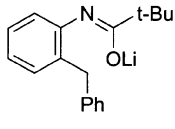
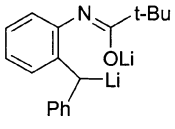
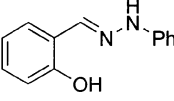
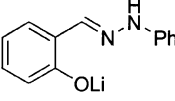
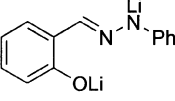
Chart 1.1 The Hoffmann test

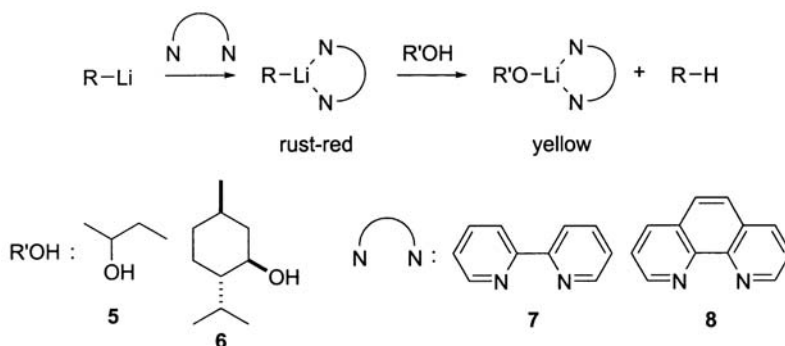
1.2.4

Titration of Organolithium Compounds

One can easily and reliably check the identity, purity, and concentration of an organolithium compound in solution by several methods. One of the most standard methods is titration of the organolithium solution with alcohols such as 2-butanol (**5**) or (–)-menthol (**6**) in the presence of a small amount of 2,2'-bipyridine (**7**) or 1,10-phenanthroline (**8**) as a color indicator. This method is based on the color difference between the C–Li and O–Li compounds, with the ligands used as color indicators (Scheme 1.2). For example, addition of a spatula tip of **8** to a solution of an organolithium species in an ether or a hydrocarbon produces a characteristic rust-red charge-transfer (CT) complex. Titration with a standardized solution of **5** in xylene until complete decoloration enables determination of the concentration of the organolithium compound [20]. To minimize the experimental complexity a variety of indicators [21–25] bearing a functional group to coordinate to lithium and another to develop a color within the same molecule have been developed, as shown in Tab. 1.4. However, one should select appropriate color indicators depending on the structure of the organolithium compounds that correlate with the sharpness of color development.

Tab. 1.4 Color indicators in titration

Color indicator	Color change	Suitable RLi	Reference
	 colorless	 yellow	MeLi n-BuLi [21]
	 colorless	 orange	MeLi n-BuLi t-BuLi PhLi [22]
	 colorless	 orange red	MeLi n-BuLi s-BuLi t-BuLi [23]
	 colorless	 bright yellow	n-BuLi s-BuLi t-BuLi [23]
	colorless	deep red	n-BuLi s-BuLi t-BuLi [23]
	 colorless	 yellow orange	MeLi n-BuLi s-BuLi t-BuLi PhLi [24]
	 yellow	 red	MeLi n-BuLi t-BuLi [25]



Scheme 1.2

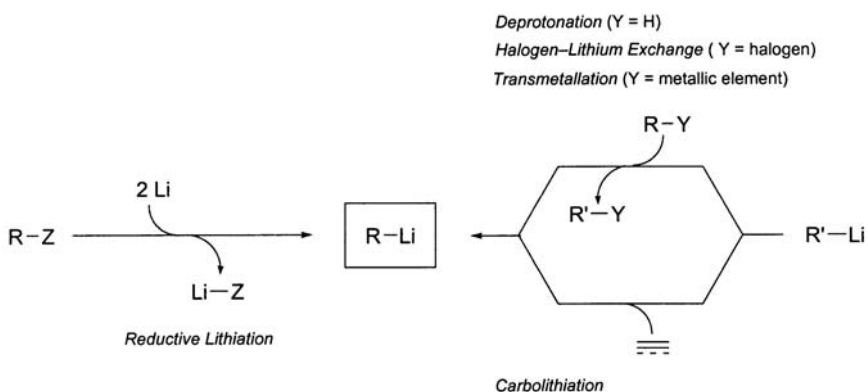
1.3

Methods for the Preparation of Organolithium Compounds

1.3.1

Overview

A C–Li bond can be created by one of two principally different methods. One is the de novo creation of C–Li bonds in which the lithium metal undergoes reductive insertion to an organic compound with the leaving group Z; the other involves construction of new C–Li bonds by another organolithium reagent (Scheme 1.3). The former method, detailed in Section 1.3.2, is still the most straightforward and often also the most rational approach; it is therefore used in the industrial production of typical organolithium compounds. The latter method



Scheme 1.3